Remarks

The Office Action dated November 5, 2008 has been carefully reviewed and the following comments are made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Without prejudice or disclaimer and for the sole purpose of advancing prosecution, Applicants have amended the claim to recite that the methods are directed to Hendra virus or Nipah virus. As a result of this amendment, Applicants have canceled certain claims and amended others to simplify the claim structure. Furthermore, without acquiescing to the merits of any rejection or objection and for the sole purpose of advancing prosecution, Applicants have amended claim 39 as suggested by the Examiner. No new matter has been added by this amendment.

The Claim Objections should be withdrawn

Without acquiescing to the merits of the objection and for the sole purpose of advancing prosecution, Applicants have amended claim 39 as requested by the Examiner thereby rendering the claim objection moot. Furthermore, the objections to claims 19, 26, and 42 are moot in light of the claim amendments.

The Rejections under 35 U.S.C. 112 should be withdrawn

A. Claims 16 to 19 were rejected under 35 U.S.C. 112, first paragraph for allegedly lacking enablement. Without prejudice or disclaimer and for the sole purpose of advancing prosecution, Applicants have amended claim 16 to recite that the paramyxovirus is a Hendra virus or Nipah virus. As amended and as indicated in the Office Action, the claims are "enabling for the fusion of Nipah and Hendra viruses" (*see* Page 2 of the Office Action) and therefore this rejection is moot.

B. Claim 39 was rejected under 35 U.S.C. 112, first paragraph for allegedly lacking enablement. Without prejudice or disclaimer and for the sole purpose of advancing prosecution, Applicants have amended claim 39 to recite an immunogenic composition. Since the specification is enabling for an immunogenic composition (*see* Page 2 of the Office Action), this rejection is moot.

The Rejections under 35 U.S.C. 103(a) should be withdrawn

A. Claims 16, 18, 19, 23 to 26, 31 to 38, 40 to 43, 45 and 46 were rejected under 35 U.S.C. 103(a) as allegedly being obvious over (1) U.S. Patent 5,843,451 to Compans and Ranjit ("Compans") (2) Lambert *et al.* (3) Young *et al.*, (4) Williamson *et al.* and (5) Harcourt *et al.*

The crux of the obviousness rejection is that Lambert *et al.* and Young *et al.* provide the basis for testing F proteins of paramyxoviruses for potential inhibitory properties of viral fusion and that therefore one of skilled in the art would be capable of testing fragments of the F protein of Nipah or Hendra virus for their inhibitory effects since this would only require substitution of a known sequence (page 8 of the Office Action). Accordingly, these claims are alleged to be obvious.

Applicants respectfully disagree. As the Examiner is aware the scope and content of the prior art is determined based on what was known at the time of the invention (M.P.E.P. 2141.01). At the time of the invention, there were large differences between the prior art and the pending claims, as highlighted in the Office Action. Specifically, the Office Action indicates that:

(1) the art recognizes that Hendra and Nipah viruses, while classified in the *Paramyxoviridae* family of virus, share limited homology with the other viruses of this family (page 3 of the Office Action);

(2) the art recognizes that there are significant amino acid differences in the fusion protein from Nipah and Hendra viruses when compared to other viruses *Paramyxoviridae* family of virus (page 3 of the Office Action);

(3) the 20 residue N-terminal end of the F-protein Hendra and Nipah virus reveals limited similarities with other viruses in *Paramyxoviridae* family of virus (page 3 of the Office Action);

(4) Nipah and Hendra possess larger species tropism with regard to cell fusion and infection which exposes how Nipah and Hendra may target different receptors compared to other paramyxoviruses(page 3 of the Office Action); and

(5) the F protein lacks homology across the species in the *Paramyxoviridae* family of virus (*see* page 3 of the Office Action).

Given these large differences those of skill in the art would not have relied upon the references cited by the Examiner. Accordingly, these large differences point to the non-obviousness of the pending claims.

None of the references cited by the Examiner disclose or suggest SEQ ID NO: 1 and/or SEQ ID NO: 2. As the Office Action indicates Compans *et al.* do not teach the administration of SEQ ID NO: 1 and/or SEQ ID NO: 2 to induce an immune response, nor do they teach Hendra or Nipah viruses (page 5 of the Office Action). Lambert *et al.* and Young *et al.* do not teach the use of SEQ ID NO: 1 and/or SEQ ID NO: 2 or the inhibition of cell fusion by a virus from the *Henipavirus* genus (page 5 of the Office

Action). Williamson only discloses the administration of Hendra viruses to guinea-pigs. Harcourt *et al.* only disclose a molecular characterization of Nipah and Hendra virus, including the entire F protein. In addition, none of the references cited provide any information on a potential active anti-Henipavirus fusion inhibitor. The very fact that the Examiner relies on such a large number of references points to the non-obviousness of the claimed invention and it is a clear indication of hindsight reasoning.

Those of skill in the art would not have modified the methods taught by Compans, Lambert *et al.*, and Young *et al.* to inhibit viral fusion and infection of a virus from the *Henipavirus* genus as claimed. The fragment used by Young *et al.* clearly is not of similar size as the claimed sequences. Young *et al.* uses a peptide created from a 20 amino acid fragment (Young *et al.* at abstract) of the Newcastle disease virus fusion protein, while SEQ ID NO: 1 and SEQ ID NO: 2 are more than twice as long and derived from different viruses (Hendra and Nipah). Lambert *et al.* disclose that in paramyxoviruses the fusion (F) proteins are potent inhibitors of fusion (see e.g. Lambert *et al.* at Abstract). Lambert *et al.* found several biologically active domains in the F1 region of RSV, HPIV-3, and MV (Lambert *et al.*, page 2187, column 2) and that those peptides exhibited antiviral properties in certain paramyxoviruses. Lambert *et al.* do not disclose or discuss F proteins of Henipaviruses (Nipah and Hendra). Even if these two references were to disclose the F protein, none of these references discloses or suggest that a peptide containing only a fragment of a Henipavirus F protein can be used as a fusion inhibitor. As is noted in the specification, Applicants "surprisingly discovered that the FC1 peptide [SEQ ID NO: 1] could completely inhibit HEV mediated fusion" (*see* specification page 10, lines 10 to 12 (emphasis added)). Furthermore, none of the references discloses or suggests that a synthetic peptide derived from a Henipavirus F protein can be used as a fusion inhibitor for both Hendra and Nipah (*see* specification page 10 lines 14 to 15 and page 24, line 14 to page 25, line 15). As discussed above, Hendra and Nipah viruses differ greatly from other members of the paramyxovirus family. In particular, Hendra and Nipah viruses are highly virulent BSL4 level pathogens. Furthermore, unlike most other members of the paramyxovirus family, Hendra and Nipah viruses cause a systemic disease with an incubation period that lends itself to potential therapeutic intervention with fusion inhibitors. Thus, given these large differences, there would be no reasonable expectation of success to combine the teachings of (1) Compans (2) Lambert *et al.* (3) Young *et al.*, (4) Williamson *et al.* and (5) Harcourt *et al.*

B. Claims 23 to 26, 31 to 38 and 40 to 46 were rejected under 35 U.S.C. 103(a) as being allegedly obvious over (1) Compans, (2) Young *et al.*, (3) Williamson *et al.*, (4) Harcourt *et al.* and (5) Bembridge *et al.*

Applicants respectfully disagree. Again, the large number of references relied upon by the Examiner are a clear indication of hindsight reasoning. This hindsight reasoning is particularly evident since the Examiner merely substituted one reference to find an entirely new ground of rejection.

As discussed above, as the Office Action indicates, there are large differences between Henipaviruses (Nipah and Hendra) and the other paramyxoviruses. Due to these large differences, those of skill in the art would not be motivated to combine the references cited by the Examiner.

None of the references disclose or suggest SEQ ID NO: 1 or SEQ ID NO: 2. Furthermore, none of the references discloses or suggests that SEQ ID NO: 1 or SEQ ID NO: 2 can be used as a fusion inhibitor for both Hendra and Nipah (*see* specification page 24, line 14 to page 25, line 15). The Office Action admits that Compans, Young *et al.*, Williamson *et al.* and Harcourt *et al.* do not teach the administration of a fusion protein having SEQ ID NO: 1 or SEQ ID NO: 2. Bembridge *et al.* discloses the administration of a plasmid containing the full-length fusion protein. In fact, none of these references disclose or suggest methods of inhibiting fusion of a Henipavirus with cells, as claimed.

The combination of the references does not render the pending claims obvious. In particular, given the disclosure of a viral glycoprotein subunit vaccine (Compans), a peptide inhibitor derived from the New Castle Disease Virus (Young *et al.*), methods of administering Henipaviruses to guinea pigs and fruit bats (Williamson *et al.*) and the entire F protein of Nipah and Hendra, those of skill in the art would not be motivated to design a unique 41 amino acid inhibitor of Henipaviral fusion. As highlighted in the Office Action (*see* page 3), there are numerous large differences between Henipaviruses (Hendra and Nipah) and other paramyxoviruses. Given these differences, those of skill in the art would not be motivated to apply the disclosure of F fusion proteins in other paramyxoviruses to derive the unique peptides disclosed and claimed in the instant application. These large differences also do not provide one of skill in the art with a reasonable expectation of success.

Furthermore, for both obviousness rejections, Applicants submit that since the secondary references relied upon by the Examiner do cure any of the deficiencies of the primary references, the obviousness rejections should be withdrawn.

As discussed above, contrary to the state of the art, Applicants surprisingly discovered that a synthetic peptide derived from Hendra virus can inhibit Hendra virus fusion and such a fragment is also able to inhibit Nipah virus fusion (*see* specification page 10, lines 8 to 16). Applicants further surprisingly discovered that synthetic peptide derived from Nipah virus can inhibit Nipah virus fusion and such a fragment is also able to inhibit Hendra virus fusion (*see e.g.* specification page 25, lines 1 to 4).

None of the references cited by the Examiner discloses or suggests such cross-reactivity. These surprising results further support the conclusion that the instant claims are not obvious.

In light of the foregoing arguments and amendments, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. 103(a).

Conclusion

It is respectfully submitted that all claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of the claims.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any necessary fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17, which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310.

Respectfully submitted,
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